

Amendments to the Claims:

Please cancel claim 9 without prejudice.

Please amend claim 1 as follows.

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of the Claims

1. (Currently Amended) In a method of analyzing the production of one or more selected metabolites of a biochemical reaction network producing metabolites, the method having as inputs

reactions of the biochemical reaction network constructed from genomic and biochemical data,

exchange fluxes on such of the produced metabolites as are of interest as inputs and outputs to the network,

a stoichiometric matrix, developed from the reactions and including in consideration of the exchange fluxes, defining participation of each network metabolite in each reaction and exchange flux of the network, and

a system of linear equations and inequalities defining the network, the method serving to when removed from the mathematically identify deletion sets of reactions that, network, eliminate the capability of the network to produce a selected metabolite an improvement to the method comprising:

where linear equations and inequalities of the network mathematically form a convex solution space called a flux cone calculating generating vectors of the flux cone, which generating vectors are called extreme pathways; and

using the generating vectors called extreme pathways, to determine sets of reactions that, when deleted, diminish capability of the network to produce an output metabolite of interest;

wherein the determined reaction sets correspond to critical reactions of the network which, when stopped, affect the capability of the network to produce the output metabolite of interest.

2. (Original) The method according to claim 1 that, after the determining of sets of reactions, further comprises:

selecting from the determined sets of reactions those sets that totally eliminate the capability of the network to produce the output metabolite of interest;

wherein the selected sets are called deletion sets because deletion of the reactions represented by the pathways of these sets suffices to totally eliminate the production of the output metabolite of interest by the network.

3. (Original) The method according to claim 1 wherein the calculating of the generating vectors of the flux cone is by mathematical process of convex analysis.

4. (Original) The method according to claim 3 wherein the mathematical process of convex analysis comprises: calculating any of (i) a conical basis, (ii) a convex basis, (iii) a linear basis, or (iv) a combination of any of conical and convex and linear bases.

5. (Original) The method according to claim 1 wherein at least some of the constructed reactions will have an associated constraint upon the direction in which the reaction can proceed.

6. (Original) The method according to claim 1 wherein the output of interest functional properties of interest in production network; wherein the reaction sets show consists one or more the analyzed biochemical how these more one functional properties of interest can be diminished or eliminated.

7. (Original) The method according to claim 6 wherein the output of interest consists of one functional property of interest in the analyzed biochemical production network;

wherein the reaction sets show how this functional property of interest can be diminished or eliminated.

8. (Original) The method according to claim 1
wherein the biochemical reaction network analyzed represents a disease producing, pathogenic, organism; and
wherein the metabolite of interest is necessary for survival of the pathogenic organism; and wherein the method further comprises:
using the reaction set to target development of a drug that, by obstructing those reactions of the pathogenic organism that produce the metabolite necessary for survival of the organism, serves to eliminate the pathogenic organism.

9. (Canceled) A drug developed in accordance with the method of claim 8.

10. (Withdrawn) The method according to claim 1
wherein the biochemical reaction network analyzed represents a disease producing, pathogenic, organism; and
wherein the metabolite of interest, produced by the pathogenic organism, is deleterious, inducing disease; and wherein the method further comprises:
using the reaction set for targeting the development of a drug that, by obstructing those reactions of the pathogenic organism produce the metabolite that induces disease, serves to eliminate the deleterious, disease-causing, function of the pathogenic organism.

11. (Withdrawn) A drug developed in accordance with the method of claim 10.

12. (Withdrawn) The method according to claim 1
wherein the reaction network analyzed is an organism producing desired bio-molecules of value and undesired bio-molecules of both no value; and
wherein the metabolite of interest produced by the of the undesired valueless bio-molecules;
and wherein the method further comprises:

using the reaction set to metabolically re-engineer the organism to fail of those reactions that produce the metabolite of that is undesired and valueless, therein eliminating production of undesired valueless bio-molecules while permitting production of organism is desired valued bio- molecules.

13. (Withdrawn) A metabolically re-engineered organism developed in accordance with the method of claim 12.

14. (Withdrawn) The method according to claim 1
wherein the reaction network analyzed is an organism producing both desired bio-molecules of value by multiple metabolic routes; and
wherein the metabolite of interest is produced by one of the routes of the organism; and
wherein the method further comprises:
using the reaction set to metabolically re-engineer the organism to fail of those reactions that produce the metabolite of interest via the one route, therein by eliminating production of metabolite via this route, nonetheless that the metabolite is of value, leaving intact production of the same metabolite by alternative ones of the multiple metabolic routes.

15. (Withdrawn) A metabolically re-engineered organism developed in accordance with the method of claim 14

wherein the using of the generating vectors is to determine sets of reactions that, when deleted eliminate capability of the network to produce an output metabolite of interest;

17. (Withdrawn) A method of using the mathematical process of convex analysis where a convex hull defined and spanned by unique generating, or edge, vectors is analyzable to derive a particular solution that is, mathematically, a particular point described by a flux vector lying within the interior of the convex hull,

to the purpose of identifying critical points in cellular metabolic networks engaging in biochemical reactions so that, by identification of some critical point, the particular set of complex pathways of biochemical reactions leading to this point may be better understood so that, by better understanding this set of complex pathways, it may further be better understood

which reactions, and associated pathways, can be disrupted so as to defeat that the cellular metabolic network should attain this critical point,

the method comprising:

using the convex hull to represent the capabilities of a metabolic genotype

where the unique generating, edge, vectors that define and that span the hull represent systemically independent extreme pathways of the metabolic, life, processes of the metabolic genotype, and

where every point in the hull is some non-negative combination of the unique generating, edge, vectors corresponding to the fact that every metabolic, life, process of the metabolic genotype is some combination of the extreme pathways of these metabolic processes;

mathematically solving the convex hull by process of convex analysis to derive a particular solution that represents a metabolic phenotype

where the particular solution is, particular point described by a flux vector interior of the convex hull; and

repeating the mathematically solving until a complete set of particular solutions, corresponding to a set of flux vectors each lying within the convex hull, is derived which set of solutions corresponds to all the pathways by which a particular metabolic phenotype is realized;

wherein derivation of all pathways by which the particular metabolic phenotype is realized is tantamount to recognition of all the biochemical reactions that, as part of any pathways, lead to the particular metabolic phenotype; and

wherein recognition of all biochemical reactions variously leading to the particular metabolic phenotype permits better understanding of what biochemical reactions of the metabolic genotype can be in particular disrupted so as to cause that the metabolic genotype is unable to realize the particular solution.

18. (Withdrawn) The method according to claim 17 employed on the genotype of a pathogenic, disease-causing, organism wherein the method further comprises:

developing drugs that, by obstructing those biochemical reactions of the genotype of the pathogenic organism that lead to a particular, disease - inducing, solution of the genotype, serve to eliminate the deleterious , disease-causing, phenotype of the pathogenic organism.

19. (Withdrawn) A drug developed in accordance with the method of claim 18.

20. (Withdrawn) The method according to claim 18 employed on the genotype of an organism producing both desired bio-molecules of value and undesired bio-molecules of no value, wherein the method further comprises:

metabolically re-engineering the organism so as to obstruct those biochemical reactions of the genotype of the pathogenic organism that lead to that particular solution where the phenotype produces the undesired valueless bio-molecules, eliminating production of these undesired valueless bio-molecules while permitting continued production of desired valued bio-molecules.

21. (Withdrawn) A metabolically engineered organism developed in accordance with the method of claim 20.

22. (Withdrawn) A method of analyzing a metabolic network comprising:
identifying all biochemical reactions occurring in the metabolic network, including any directions thereof;

specifying all exchange fluxes, including any associated directional restraints, attendant upon metabolites of the identified biochemical reactions;

creating a stoichiometric matrix where each column in the matrix corresponds to a reaction, or flux, and where each row corresponds to a different metabolite involved in the metabolic network;

wherein the created stoichiometric matrix represents, in all its columns and rows, the collective biochemical reactions, being form of chemical conversion and the collective cellular transport processes of the metabolic network, which cellular processes are how the metabolites enter and leave the network;

combining all directional constraints on the exchange fluxes with the created stoichiometric matrix to define the metabolic network as a system of linear equations and linear inequalities; and

analyzing the system of linear inequalities that jointly define the mathematical process of convex analysis. equations metabolic and linear network

23. (Withdrawn) The method according to claim 22 wherein the metabolic network defined as a system of linear equations and linear inequalities obeys the three equations

$$S \bullet v = 0$$

where S refers to the stoichiometric matrix of the system and v is the flux vector;

$$v_i \geq 0, \forall i$$

where v_i corresponds to the flux value of the i^{th} reaction; and

$$\alpha_i \leq b_i \leq \beta_i.$$

24. (Withdrawn) The method according to claim 23 wherein the analyzing comprises:

solving the equations 1-3 in convex polyhedral flux cone in n-dimensional space emanating from the origin of the space.

25. (Withdrawn) The method according to claim 24 wherein every point on the convex polyhedral flux cone is represented by

$$C = \{v: v = \sum_{i=1}^k \omega_i p_i, \omega_i \geq 0 \forall i\}$$

26. (Withdrawn) The method according to claim 25 wherein the analyzing further comprises: calculating extreme pathways in the metabolic represented by a conical hull of the flux cone. network as being

27. (Withdrawn) The method according to claim 26 that, after the calculating that is part of the analyzing, further comprises: determining from the calculated pathways critical biochemical reactions, or sets of biochemical reactions, that are required for the metabolic network to attain a particular objective represented by a particular point on the flux cone.